of submaximal doses of MEN16132 (1 μg/25 μl) and dexamethasone (10–30 μg/25 μl), each producing a mean 20–25% inhibition of pain, caused analgesia of about 40–45%, ascribable to the sum of the respective antinociceptive effects.
Conclusion: Intra-articular combination of low doses of MEN16132 and dexamethasone induces an additive increase of analgesia that might allow to reduce the doses of corticosteroids for the treatment of pain and inflammation associated to diseases such as osteoarthritis.
Disclosure of interest: None declared.

Neuroinflammation: central and peripheral nervous systems

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MMP-9 LEVELS IN AMYOTROPHIC LATERAL SCLEROSIS: EMERGING EVIDENCE FOR NEUROINFLAMMATION

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Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease affecting the motor neurons of the spinal cord and brain. Degeneration of spinal motor neurons leads to muscular atrophy and weakness without accompanied sensory changes, whereas degeneration of motor neurons in the cerebral cortex leads to hyper-reflexia. Because of its rapid and progressive clinical course, ALS patients generally die within 2–5 years of onset. Matrix metallo proteinases (MMPs) are a relatively large family of more than 20 Zn^{2+}- containing, Ca^{2+}-requiring endopeptidases, characterized by their ability to digest components of the extracellular matrix. Excessive expression of MMPs may result in tissue damage. Therefore, precise control of the regulation of expression and activity of MMPs is important physiologically and pathologically. ALS patients were selected using the World Federation of Neurology (WFN) clinical criteria. Elisa kit for the estimation of MMP-9 was obtained from R&D Systems, Minneapolis, MN, USA and was measured as per the manufacturer's specifications. Standard curve was prepared as per the instructions and the MMP-9 levels were expressed as ng/ml. Results show that the neuroinflammatory marker, MMP-9 levels in the serum of ALS patients were significantly ($P < 0.01$) increased with respect to control subjects and also showed significant correlation ($R^2 = 0.9$) with the duration of the disease. Neuroinflammation can both be a cause, and a consequence of chronic oxidative stress which is produced by glutamate excitotoxicity. Cytokine-stimulated microglia generate copious amounts of reactive oxygen and reactive nitrogen species, creating a stress upon ambient neurons. Conversely, oxidants can stimulate pro-inflammatory gene transcription in glia, leading to various inflammatory reactions including production of MMP-9.
Disclosure of interest: None declared.

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NAAG REDUCES NEUTROPHIL INFILTRATION AND EDEMA RESPONSE IN CARRAGEENAN-INDUCED ACUTE INFLAMMATION

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Introduction: *N*-Acetylaspartylglutamate (NAAG) is widely distributed peptide transmitter in the mammalian nervous system, activates mGlu3 receptors at presynaptic sites which results to inhibit glutamate release. Evidence suggests that glutamate receptors are involved in inflammatory response carried through the COX-2 up regulation. In present study we aimed to investigate the effect of NAAG (10 mg kg^{-1}) on carrageenan-induced acute inflammation.
Methods: Acute inflammation was induced by subplantar injection of carrageenan 1% (w/v), in the right hind paw of the rats. The animals received an intraperitoneal injection of NAAG 20 min before induction of inflammation. The severity of inflammation was assessed 4 h later using maximum paw edema volume, Area Under Curve(AUC), microscopic changes of inflamed paw, measurement of oxidative stress markers; myeloperoxidase(MPO), lipid peroxidation(MDA level), SOD and GPx activity in paw tissue.
Results and conclusion: NAAG reduced maximum inflammatory response and AUC by 52.56 and 58% ($P < 0.001$), respectively, compare to control. Microscopic studies indicated significant reduction in neutrophil infiltration. MPO activity in NAAG treated group was inhibited by 80.19% ($P < 0.01$) and MDA level was decreased by 88.13% ($P < 0.01$) compare to controls, but there were no significant reduction in SOD and GPx activity. The results, for the first time, suggest that NAAG may be involved in inhibiting peripheral inflammation and it is possible that exerts this effect by modulating systemic glutamate levels.
Keywords: *N*-acetylaspartylglutamate, inflammation, myeloperoxidase, carrageenan.
Disclosure of interest: None declared.

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THE EFFECT OF NEUROPEPTIDES AND BICYCLIC MONOTERPENE DIOLS ON NITRIC OXIDE

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Nitric oxide (NO) is an important signaling messenger with a broad range of functions in both the central and peripheral nervous systems. In the skin, NO is involved in vasodilation, melanogenesis, and immune/inflammatory processes. NO is synthesized from L-arginine by 3 isoforms of NO synthase (NOS)—neuronal NOS (nNOS), inducible NOS (iNOS), and endothelial NOS (eNOS). Keratinocytes constitutively express nNOS and can be induced to express iNOS by inflammatory cytokines. Preliminary studies using human immortalized keratinocytes (hTERT) demonstrates that iNOS is induced in a time- and dose-dependent manner by UVB and cytokines such as CGRP, substance P, and VIP. To extend these findings, we selected primary cortical neurons as a primary culture paradigm with cellular lineage distinct from keratinocytes. Expression of all NOS isoforms following neuropeptide treatment (24 vs. 48 h) was assessed by Western blot. Primary cortical neurons were treated in vitro with the nociceptive neurotransmitter substance P or bicyclic monoterpene diols (BMTd) reported to increase NO levels in neural crest-derived cells and compared to neurons that received brain-derived neurotrophic factor (BDNF, 100 ng/μl), a growth